

Remarks

I. Status of the claims

Claims 1-2, 8, 15, 29-31, 53, 55-59, 61-66, 91-92 and 96-104 are pending in this application. The amendments are intended to remove non-elected subject matter from the claims. The claims now pending should recite the scope of subject matter examined. Claim 104 recites a specific compound more broadly covered by at least claims 1 and 102.

The undersigned expresses appreciation to the Examiner for discussing the restriction requirement by telephone on October 15, 2002. Applicants respectfully request that the Examiner modify the restriction and examine the invention where variable a is 0-6 and variable b is 0-4, as opposed to both a and b defined as 1. If a compromise is necessary, applicants respectfully request that the Examiner modify the restriction to examine the invention where variables a and b are at least independently 0 or 1.

Applicants have amended the definition of variable Ar I in claim 1 as requested by the Examiner. Amendments to claims 2 and 3 were also made in light of the amendment to claim 1. Applicants have also made explicit that certain groups recited in the claims are optionally substituted. This was already understood from the definitions of those groups in the specification.

The amendments made to the claims appear in Appendix A. For the Examiner's convenience, applicants also include in Appendix B a clean copy of all claims now pending after the amendments made above.

II. Objection to claim 30

The Examiner objected to claim 30 for lacking commas in two locations of the claim. The amendment to claim 30 should resolve this issue.

III. Rejections under 35 U.S.C. § 102

The Examiner rejected claims 1-2, 15, 29-31, 53, 91, 92, 102 and 103 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,290,973 to Hawkins et al. ("Hawkins"). In support of the rejection, the Examiner particularly identified the two

compounds appearing at col. 61, lines 35-45 of that document. Applicants respectfully traverse this rejection.

The compound appearing at line 45 of the cited portion of Hawkins does not appear to contain any group that would correspond to group Ar II of the claimed invention, which is an optionally substituted phenyl group.

The compound appearing at line 40 of the cited portion of Hawkins contains a substituted 4,5-dihydro-oxazole, or 2-oxaline group, in the position corresponding to group Ar I of the claimed invention. Group Ar I in the present claims is an optionally substituted heteroaryl. The specification at page 12, line 15, defines "heteroaryl" as an aromatic ring system. The 4,5-dihydro-oxazole, or 2-oxaline group, of Hawkins, however, is not aromatic and is therefore not a heteroaryl group.

For at least the reasons given above, the cited compounds do not anticipate the claimed invention. The claimed invention is also non-obvious over the cited compounds, as Hawkins and the art generally would not have suggested modifying the compounds in ways necessary to reach the invention.

IV. Rejection under 35 U.S.C. § 112

The Examiner rejected claim 54 under 35 U.S.C. § 112, first paragraph, as non-enabled. The Examiner did acknowledge, however, that claims 55-59 and 61-66, which depend from claim 54, recite allowable subject matter. Although applicants disagree that claim 54 is non-enabled, that claim has been canceled and claims 55-59 and 61-66 have been rewritten so as to not depend from claim 54. In light of these amendments, the rejection of claim 54 should be moot.

Application No. 09/662,649
Attorney Docket No. 02481.1690

If there is any fee due in connection with the filing of this Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

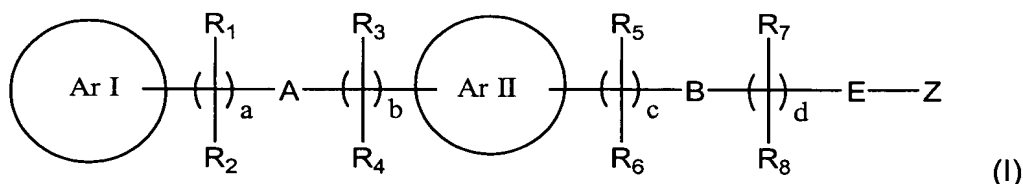
FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Date: November 7, 2002

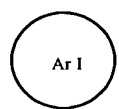
By: Steven J. Scott Reg. No. 43,911
for Steven J. Scott Reg. No. 43,911

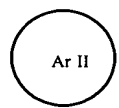
Appendix A: Current Amendments to Claims

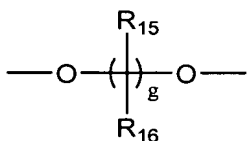
1. (Four Times Amended) A compound of formula (I)



wherein:

 is [fused arylheterocyclenyl, fused arylheterocyclyl,] heteroaryl, [fused heteroarylcycloalkenyl, fused heteroarylcycloalkyl, fused heteroarylheterocyclenyl, or fused heteroarylheterocyclyl, all of] which is [are] optionally substituted;

 is optionally substituted phenyl;



B and E are a chemical bond;

a is 0-6;

b is 0-4;

c is 0;

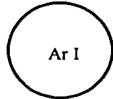
d is 0;

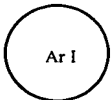
g is 1-5;

R₁, R₂, R₃ and R₄ are, independently, hydrogen, halogen or optionally substituted alkyl;

Z is R₂₁O₂C-, R₂₁OC-, -CN, R₂₁O₂SHNCO-, R₂₁O₂SHN-, (R₂₁)₂NCO- or R₂₁O-; and R₂₁ is independently hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted cycloalkyl, or optionally substituted aralkyl;

R₁₅, R₁₆ are independently hydrogen, optionally substituted alkyl, optionally substituted aralkyl, carbonyl, or optionally substituted alkoxycarbonyl; or a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

2. (Twice Amended) A compound according to claim 1 wherein  is optionally substituted azaheteroaryl [, or optionally substituted fused arylheterocyclenyl or optionally substituted fused arylheterocyclyl].

30. (Three Times Amended) A compound according to claim 1 wherein  is an optionally substituted quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, N-alkyl-quinolin-4-onyl, quinazolin-4-onyl, benzoxazolyl, benzimidazolyl, benzothiazolyl, benzofuranyl, benzothiophenyl, [indolinyl] oxazolyl, thiazolyl, oxadiazolyl, isoxazolyl, imidazolyl, pyrazolyl [pyrazol-yl], thiadiazolyl, triazolyl, pyridyl, pyrimidinyl, pyrazinyl or pyridazinyl group, wherein the substituent is a ring system substituent.

55. (Three Times Amended) A method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound [according to claim 54] wherein the disorder is associated with a physiological detrimental blood level of insulin, glucose, free fatty acids, or triglycerides.

56. (Amended) A [The] method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound [according to claim 54], wherein the physiological disorder is hyperglycemia.

59. (Amended) A [The] method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound [according to claim 54], wherein the physiological disorder is hyperinsulinism.

61. (Amended) A [The] method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound [according to claim 54], wherein the physiological disorder is insulin resistance.

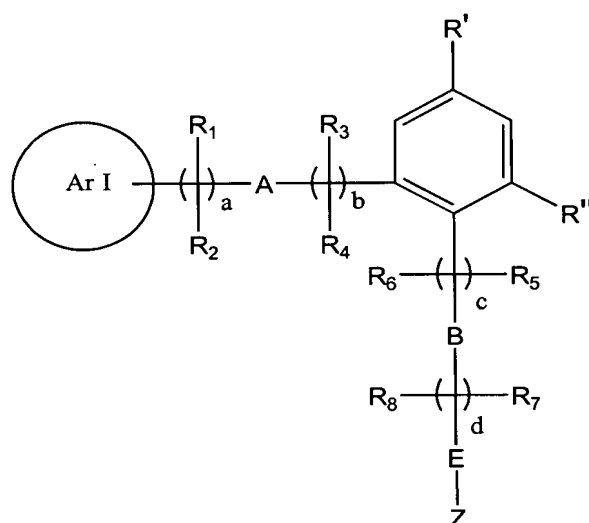
62. (Amended) A [The] method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound [according to claim 54], wherein the physiological disorder is a cardiovascular condition.

64. (Amended) A [The] method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound [according to claim 54], wherein the physiological disorder is hyperlipidemia.

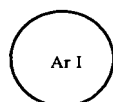
65. (Amended) A [The] method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound [according to claim 54], wherein the physiological disorder is hypertension.

66. (Amended) A [The] method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound [according to claim 54], wherein the physiological disorder is an eating disorder.

97. (Twice Amended) A compound as claimed in claim 1, which is of formula



wherein

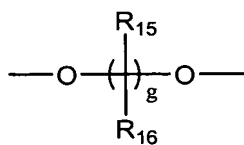


is optionally substituted heteroaryl;

$a = 1$;

$b = 0$;

R_1, R_2, R_3, R_4 are hydrogen



A is ;

R_{15}, R_{16} are hydrogen;

$c = 0$;

$d = 0$;

D

$g = 2, 3, 4$ or 5 ;

B and E are a chemical bond;

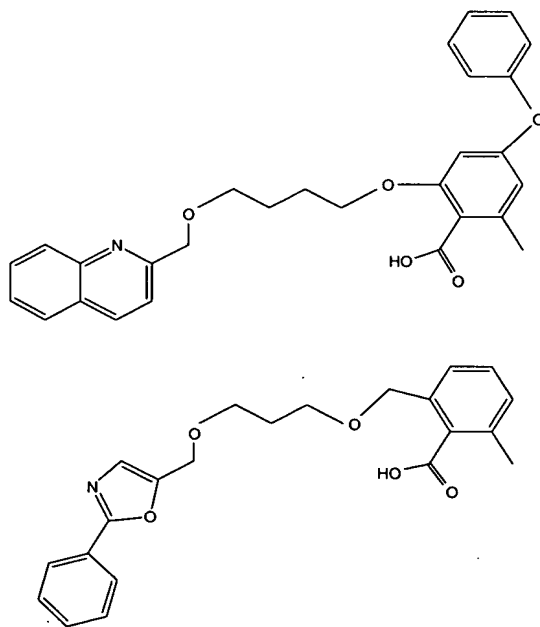
Z is $R_{21}O_2C-$, $R_{21}OC-$, or $R_{21}O-$;

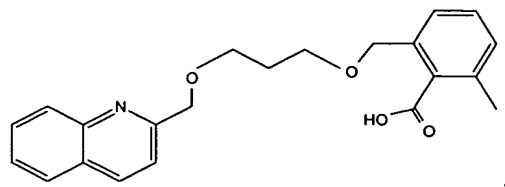
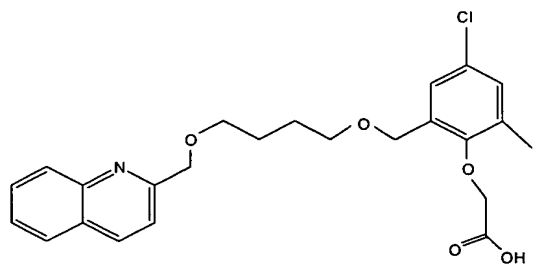
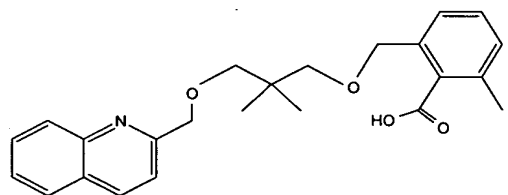
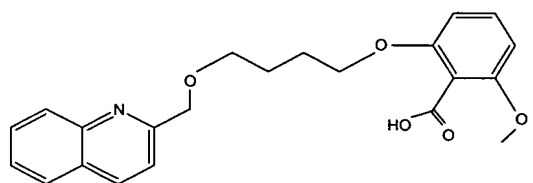
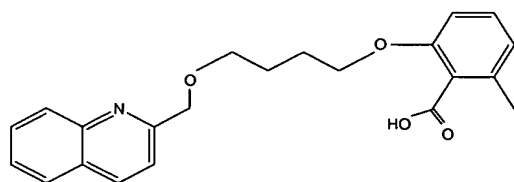
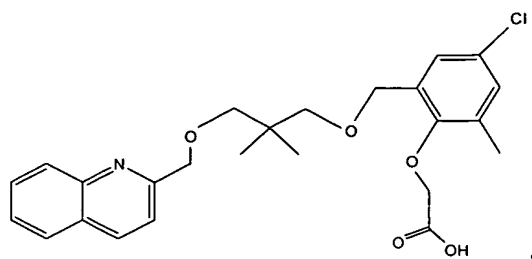
R_{21} is hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted cycloalkyl, or optionally substituted aralkyl;

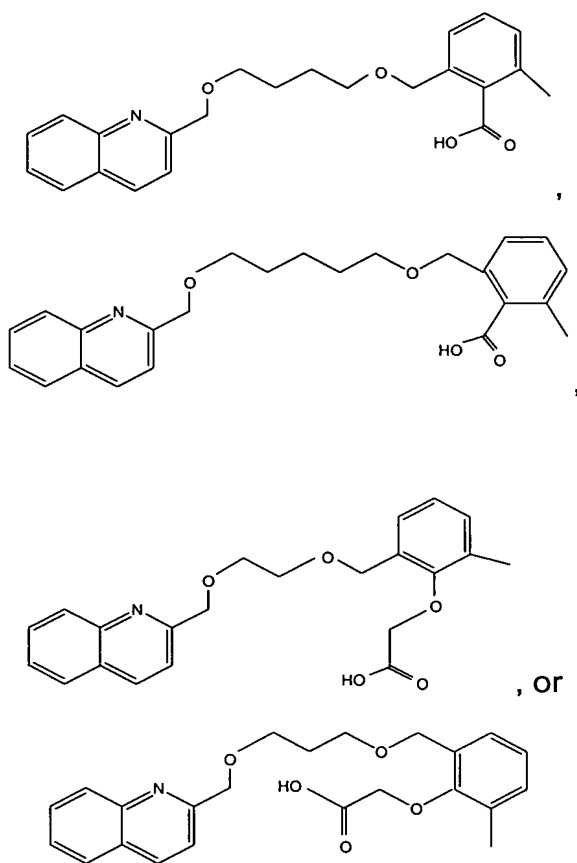
R' is hydrogen, optionally substituted lower alkyl, halo, optionally substituted alkoxy, optionally substituted aryloxy or optionally substituted aralkyloxy; and

R'' is optionally substituted lower alkyl, hydrogen, optionally substituted aralkyloxy, optionally substituted alkoxy, optionally substituted cycloalkylalkyloxy or halo, or a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

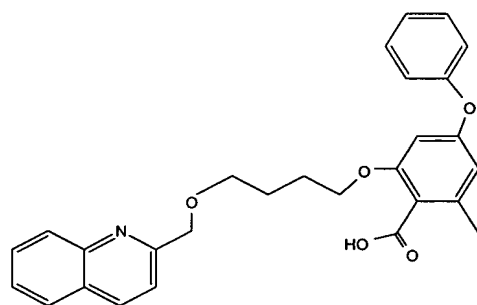
102. (Amended) A compound [the] according to claim 1, wherein the compound is





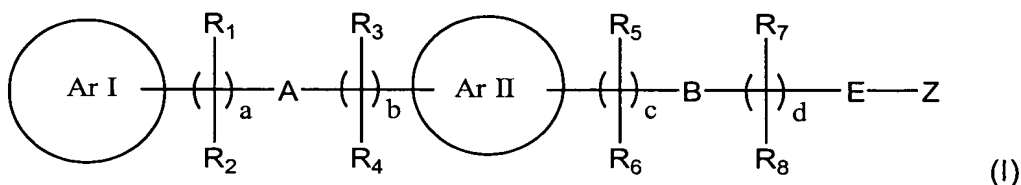


103. (Amended) A compound [the] according to claim 1, wherein the compound is

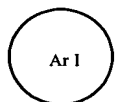


Appendix B: All Pending Claims (As Amended)

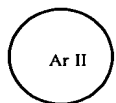
1. (Four Times Amended) A compound of formula (I)



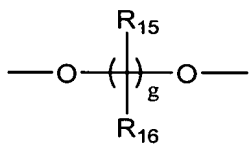
wherein:



is heteroaryl, which is optionally substituted;



is optionally substituted phenyl;



A is

;

B and E are a chemical bond;

a is 0-6;

b is 0-4;

c is 0;

d is 0;

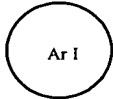
g is 1-5;

R₁, R₂, R₃ and R₄ are, independently, hydrogen, halogen or optionally substituted alkyl;

Z is R₂₁O₂C-, R₂₁OC-, -CN, R₂₁O₂SHNCO-, R₂₁O₂SHN-, (R₂₁)₂NCO- or R₂₁O-; and R₂₁ is independently hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted cycloalkyl, or optionally substituted aralkyl;

R₁₅, R₁₆ are independently hydrogen, optionally substituted alkyl, optionally substituted aralkyl, carbonyl, or optionally substituted alkoxycarbonyl;

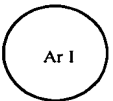
or a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

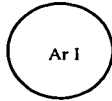
2. (Twice Amended) A compound according to claim 1 wherein  is optionally substituted azaheteroaryl.

8. (Amended) A compound according to claim 1 wherein $a = 0$; R_{15} and R_{16} are hydrogen; g is 1, 2, 3 or 4; and $b = 0$.

15. (Amended) A compound according to claim 1 wherein Z is $R_{21}O_2SHNCO^-$, and R_{21} is phenyl.

29. (Amended) A compound according to claim 1 wherein Z is $-CO_2H$ or $-CN$.

30. (Three Times Amended) A compound according to claim 1 wherein  is an optionally substituted quinoliny, quinoxaliny, quinazoliny, isoquinoliny, *N*-alkyl-quinolin-4-onyl, quinazolin-4-onyl, benzoxazolyl, benzimidazolyl, benzothiazolyl, benzofuranyl, benzothiophenyl, oxazolyl, thiazolyl, oxadiazolyl, isoxazolyl, imidazolyl, pyrazolyl, thiadiazolyl, triazolyl, pyridyl, pyrimidinyl, pyrazinyl or pyridazinyl group, wherein the substituent is a ring system substituent.

31. (Twice Amended) A compound according to claim 1 wherein  is unsubstituted quinolin-2-yl, 3-substituted quinolin-2-yl, 4-substituted quinolin-2-yl, 6-substituted quinolin-2-yl or 7 substituted quinolin-2-yl; an unsubstituted quinoxalin-2-yl, 3-substituted quinoxalin-2-yl, 6-substituted quinoxalin-2-yl or 3,6-disubstituted quinoxalin-2-yl; unsubstituted quinazolin-2-yl, 4-substituted quinazolin-2-yl or 6-

substituted quinazolin-2-yl; unsubstituted isoquinolin-3-yl, 6-substituted isoquinolin-3-yl or 7-substituted isoquinolin-3-yl; 3-substituted-quinazolin-4-on-2-yl; *N*-substituted quinolin-4-on-2-yl; 2-substituted-oxazol-4-yl or 2,5 disubstituted-oxazol-4-yl; 4-substituted oxazol-2-yl or 4,5-disubstituted-oxazol-2-yl; 2-substituted thiazol-4-yl or 2,5-disubstituted thiazol-4-yl; 4-substituted thiazol-2-yl or 4,5-disubstituted-thiazol-2-yl; 5-substituted-[1,2,4]oxadiazol-3-yl; 3-substituted-[1,2,4] oxadiazol-5-yl; 5-substituted-imidazol-2-yl or 3,5-disubstituted-imidazol-2-yl; 2-substituted-imidazol-5-yl or 2,3-disubstituted-imidazol-5-yl; 3-substituted-isoxazol-5-yl; 5-substituted-isoxazol-3-yl; 5-substituted-[1,2,4] thiadiazol-3-yl; 3-substituted-[1,2,4]-thiadiazol-5-yl; 2-substituted-[1,3,4]-thiadiazol-5-yl; 2-substituted-[1,3,4]-oxadiazol-5-yl; 1-substituted-pyrazol-3-yl; 3-substituted-pyrazol-5-yl; 3-substituted-[1,2,4]-triazol-5-yl; 1-substituted-[1,2,4]-triazol-3-yl; 3-substituted pyridin-2-yl, 5-substituted pyridin-2-yl, 6-substituted pyridin-2-yl or 3,5-disubstituted pyridin-2-yl; 3-substituted pyrazin-2-yl, 5-substituted pyrazin-2-yl, 6-substituted pyrazin-2-yl or 3,5 disubstituted-pyrazin-2-yl; 5-substituted pyrimidin-2-yl or 6-substituted-pyrimidin-2-yl; 6-substituted-pyridazin-3-yl or 4,6-disubstituted-pyridazin-3-yl; unsubstituted -benzothiazol-2-yl or 5-substituted-benzothiazol-2-yl; unsubstituted benzoxazol-2-yl or 5-substituted-benzoxazol-2-yl; unsubstituted -benzimidazol-2-yl or 5-substituted-benzimidazol-2-yl; unsubstituted -thiophen-2-yl, 3-substituted -thiophen-2-yl, 6-substituted -thiophen-2-yl or 3,6-disubstituted-thiophen-2-yl; unsubstituted -benzofuran-2-y, 3-substituted-benzofuran-2-yl, 6-substituted-benzofuran-2-yl or 3,6-disubstituted-benzofuran-2-yl; 3-substituted-benzofuran-6-yl or 3,7-disubstituted-benzofuran-6-yl, wherein the substituent is a ring system substituent.

53. A pharmaceutical composition comprising a pharmaceutically acceptable amount of the compound according to claim 1 and a pharmaceutically acceptable carrier.

55. (Three Times Amended) A method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound wherein the disorder is associated with a physiological detrimental blood level of insulin, glucose, free fatty acids, or triglycerides.

56. (Amended) A method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound, wherein the physiological disorder is hyperglycemia.

57. The method according to claim 56, wherein the hyperglycemia is diabetes.

58. The method according to claim 56, wherein the hyperglycemia is Type II diabetes.

59. (Amended) A method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound, wherein the physiological disorder is hyperinsulinism.

61. (Amended) A method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound, wherein the physiological disorder is insulin resistance.

62. (Amended) A method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound, wherein the physiological disorder is a cardiovascular condition.

63. The method according to claim 62, wherein the cardiovascular condition is atherosclerosis.

64. (Amended) A method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound, wherein the physiological disorder is hyperlipidemia.

65. (Amended) A method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound, wherein the physiological disorder is hypertension.

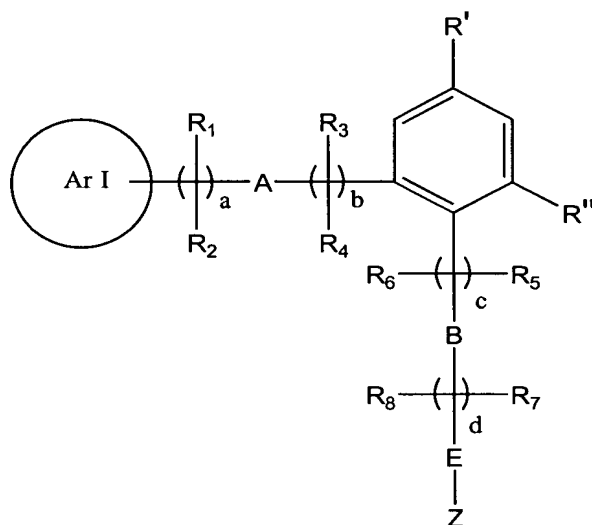
66. (Amended) A method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound, wherein the physiological disorder is an eating disorder.

91. A compound as claimed in claim 30, wherein the ring system substituent is selected from the group consisting of phenyl, substituted-phenyl, thienyl, substituted thienyl, cycloalkyl, lower alkyl, branched alkyl, fluoro, chloro, alkoxy, aralkyloxy, trifluoromethyl and trifluoromethyloxy.

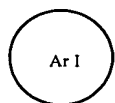
92. A compound as claimed in claim 31, wherein the ring system substituent is selected from the group consisting of phenyl, substituted-phenyl, thienyl, substituted thienyl, cycloalkyl, lower alkyl, branched alkyl, fluoro, chloro, alkoxy, aralkyloxy, trifluoromethyl and trifluoromethyloxy.

96. A compound as claimed in claim 1, wherein the compound is 2-methyl-6-[3-(quinolin-2-ylmethoxy)-propoxymethyl]-benzoic acid.

97. (Twice Amended) A compound as claimed in claim 1, which is of formula



wherein

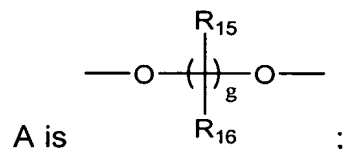


is optionally substituted heteroaryl;

$a = 1$;

$b = 0$;

R_1, R_2, R_3, R_4 are hydrogen



A is

R_{15}, R_{16} are hydrogen;

c = 0;

d = 0;

g = 2, 3, 4 or 5;

B and E are a chemical bond;

Z is $R_{21}O_2C-$, $R_{21}OC-$, or $R_{21}O-$;

R_{21} is hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted cycloalkyl, or optionally substituted aralkyl;

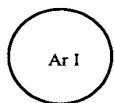
R' is hydrogen, optionally substituted lower alkyl, halo, optionally substituted alkoxy, optionally substituted aryloxy or optionally substituted aralkyloxy; and

R'' is optionally substituted lower alkyl, hydrogen, optionally substituted aralkyloxy, optionally substituted alkoxy, optionally substituted cycloalkylalkyloxy or halo, or a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

98. A compound according to claim 97, wherein Z is $-CO_2H$.

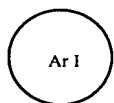
99. A compound according to claim 97, wherein R' is hydrogen; and R'' is lower alkyl.

100. A compound according to claim 97, wherein



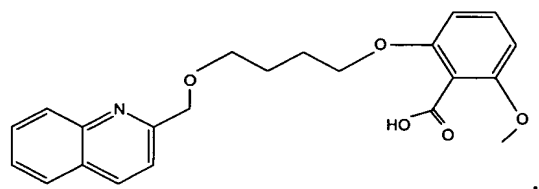
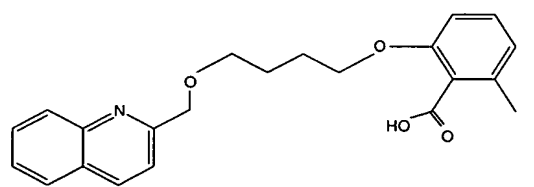
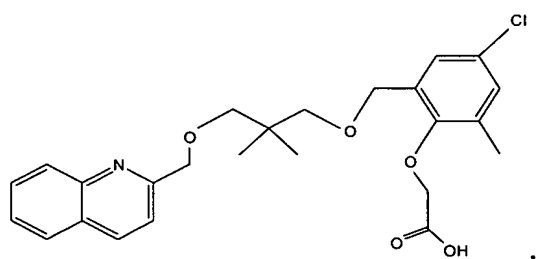
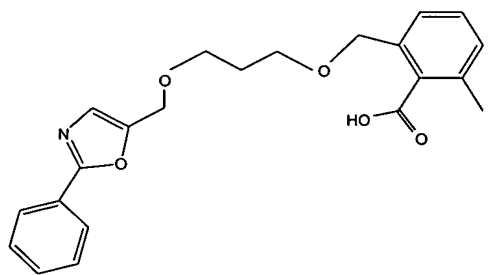
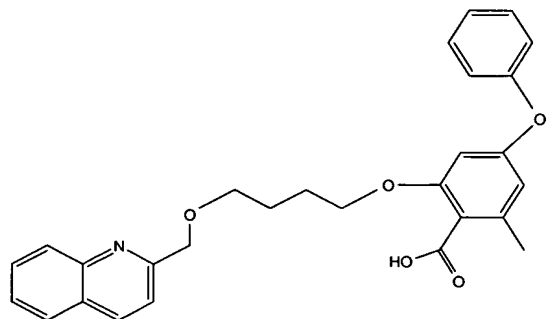
is optionally substituted azaheteroaryl.

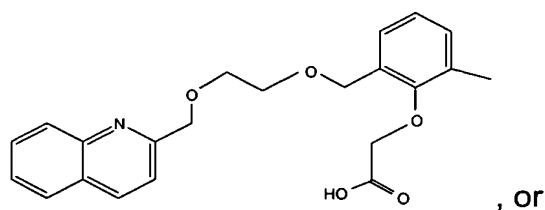
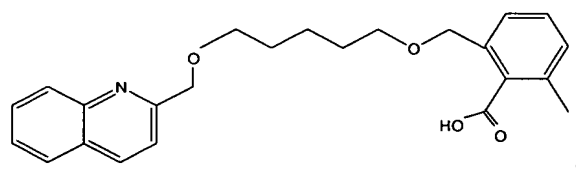
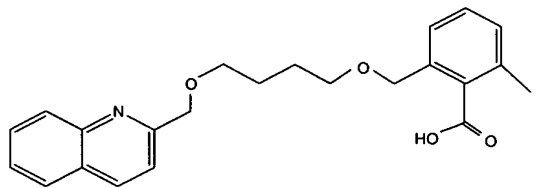
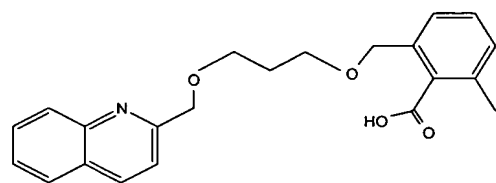
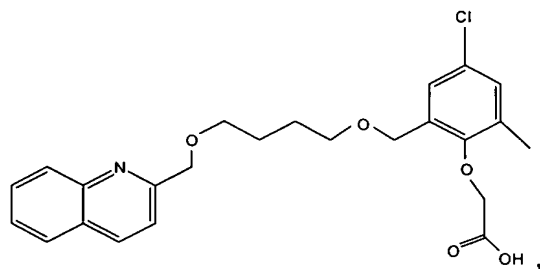
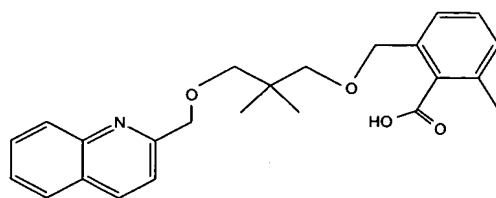
101. A compound according to claim 97, wherein



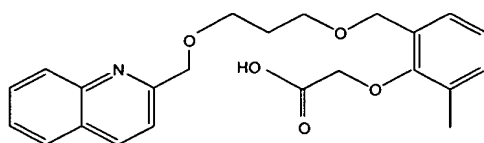
is 2-substituted-oxazol-4-yl.

102. A compound according to claim 1, wherein the compound is

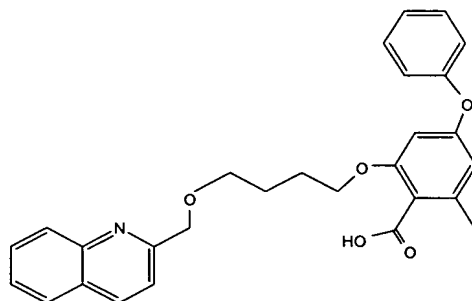




D



103. A compound according to claim 1, wherein the compound is



104. A compound according to claim 1, wherein the compound is

